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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,632	11/13/2003	Lawrence M. Kauvar	388512011000	2417

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,632	KAUVAR ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed November 20, 2006. Applicant's arguments have been fully considered. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Claims 1-17 are currently pending. Claims 1, 3, and 8-10 have been amended. Therefore Claims 1-17 will be addressed herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

In the instant case the specification does not appear to provide support for the amendment which recites a method which "does not include a step of separating the target nucleic acid from non-target nucleic acid". It is noted that the applicant points to

the specification at page 7 paragraph 0026 for support. The specification states "The present invention offers highly sensitive ways to analyze a target nucleic acid without the need for physical separation steps". This phrase could mean that the invention does not require the step of separating the target from the non target nucleic acids or it could mean that the invention does not require the step of separating unbound probes prior to detection. Thus the specification does not provide support for a method which "does not include a step of separating the target nucleic acid from non-target nucleic acid".

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17 are indefinite over the recitation of the phrase "observing by microscopy the presence or absence of proximity" in claims 1 and 8. This phrase in considered indefinite because it is unclear what defines the presence of proximity or the absence of proximity and how proximity is determined. It is unclear if the first and second probes have to hybridize within a certain number of base pairs of each other to be considered proximal. Further the claims are indefinite over the recitation of the

phrase "whereby the presence of said proximity identifies said desired region". This phrase in considered indefinite because it is unclear how the presence of proximity identifies a region. It is unclear if only probes which hybridize within a certain number of base pairs of each other are able to identify a region.

Claims 3 and 9 are indefinite over the recitation of the phrase "said first and second fluorophores". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

4. THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, 7-10, 12, 14-15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (US Patent 6475720 Filed 1995) in view of Barbera-Guillem et al (US Patent 6309701 Issued 2001).

Regarding Claims 1-3, 5, 8-10, 12, 14-15, and 17 Gray et al teach a method in which FISH probes from chromosomes 9 (BCR probe) and 22 (ABL probe) were hybridized to metaphase and interphase spreads in order to detect the BCR-ABL fusion

in chronic myelogenous leukemia (CML) (Column 58 and Fig 11 c-d). The genetic rearrangement of CML brings the DNA sequences homologous to the probes together on an abnormal chromosome. The genomic distance between the probe binding sites in the fusion gene varies among CML cases, ranging from 25 to 225kb (Column 61). The FISH was carried out using a biotin labeled ABL probe detected with the fluorochrome Texas red, and a digoxigenin labeled BCR probe detected with the green fluorochrome FITC. Hybridization of both probes could be observed simultaneously using a fluorescent microscope (Column 59). Thus Gray et al teach a method of contacting a sample with first and second probes which bracket a region and observing by microscopy the two probes. Gray et al do not teach a step of separating the target nucleic acid from non-target nucleic acid. Additionally Gray et al teach that the target nucleic acid is a human nucleic acid sequence.

Gray et al do not teach that the probes were coupled to particulate labels and that the method can be performed simultaneously on multiple targets using different probes which have different particulate labels of differing hues.

However Barbera-Guillem et al teach a method which utilizes a fluorescent microsphere (comprising fluorescent nanocrystals) coupled to nucleic acid probe to determine the presence or absence of a target nucleic acid in a sample. The target is detected by observing the fluorescence signal pattern of the excited fluorescent microsphere bound to the target using a fluorescent microscope (Abstract, Columns 2-3). Further Barbera-Guillem et al teach that this method can be used to determine the presence or absence of a single target nucleic acid or multiple target nucleic acids. In

the case where multiple targets are present different fluorescent microspheres which emit different colors are used to detect the multiple targets (Example 6).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Gray et al by using a nucleic acid probe coupled to a particulate label (i.e. a fluorescent microsphere comprising fluorescent nanocrystals) as suggested by Barbera-Guillem. Barbera-Guillem teach several advantages of using particulate labels (specifically fluorescent microspheres) over conventional fluorescent labels to detect nucleic acid hybridization. The first advantage is that the fluorescent signal produced by fluorescent microspheres is much more intense than the signal produced by conventional fluorescent labels. Additionally fluorescent microspheres have a wider excitation spectrum therefore it is possible to detect multiple fluorescent microspheres which each emit a different hue using a single wavelength spectrum of light. Further fluorescent microspheres are resistant to photo bleaching so there is no limitation on the time in which the fluorescent signal can be detected (Columns 1-2).

5. THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 4, 6, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (US Patent 6475720 Filed 1995) in view of Barbera-Guillem et al (US Patent 6309701 Issued 2001) and in further view of Nie et al (US Patent 6060242).

The teachings of Gray et al and Barbera-Guillem et al are presented above in paragraph 4.

Regarding Claims 4, 6, 11, and 13 the combined references do not teach a method wherein the first and second probes are peptide nucleic acids. Additionally the combined references do not teach a method wherein the target nucleic acid is double stranded and the probe forms a triplex with the target nucleic acid.

However Nie et al teach a method which uses a plurality of PNA probes which bind to target nucleic acid seqeucnes. Nie et al further teaches that PNA are able to recognize dsDNA and form triplex complexes with dsDNA (Column 3).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Gray et al by using PNA probes rather than DNA/RNA probes as suggested by Nie for the benefit of being able to use a probe which can recognize dsDNA and hybridize to dsDNA targets.

6. THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (US Patent 6475720 Filed 1995) in view of Barbera-Guillem et al (US Patent 6309701 Issued 2001) and in further view of Ward et al (US Patent 6506563 Filed 1999).

The teachings of Gray et al and Barbera-Guillem et al are presented above in paragraph 4.

Regarding Claim 16 the combined references do not teach that the target nucleic acid is derived from an organism wherein the organism is an infectious agent.

However Ward et al teach oligonucleotide probes which are capable of binding chromosomes. The probes taught by Ward are sufficient to permit the characterization of bacteria, viruses and/or lower eukaryotes that may be present in a clinical or non-clinical preparation (Column 2 and 29). In the instant case bacteria and viruses are being interpreted as infectious agents.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Gray et al so as to have used the probes to detect bacterial or viral nucleic acids in order to have achieved the benefits set forth by Ward of providing a method which enables one to asses the presence or absence of infectious agents by employing labeled probes specific for the bacterial or viral sequences.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

DIANA JOHANNSEN
PRIMARY EXAMINER